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PERIODONTAL LESIONS IN THE RAT INDUCED BY
X-RAYS AND NEUTRONS

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ADMINISTRATIVE INFORMATION

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ABSTRACT

Male Sprague-Dawley rats were exposed at 101 days of age to whole body doses of 430 or 680 rads of X rays or to 230, 320 or 360 rads of fast neutrons. Dental lesions, evidenced by chalky white zones in the tooth substance, began appearing at the gingival crest approximately 35 days postirradiation in the mandibular incisors and several weeks later in the maxillary incisors. The time of maximum incidence of animals with lesions occurred between the fiftieth and seventy-fifth days postirradiation and, by the end of the fourth month, all lesions had disappeared from the continually growing incisors through attrition at the occlusal edges. The total incidence of animals with one or more lesions was 97% after 430 rads of X ray and 100% after all other doses. The size of the lesions and the number of lesions per animal were greater at the higher doses for each type of radiation. In some animals fractures occurred at the lesion and were confined largely to mandibular incisors. The total incidence of animals with fractured incisors was greater at the higher doses for each type of radiation. Food in meal form, presented in open containers, resulted in a lower incidence of fractures as compared with the results of a previous study in which the same food in pellet form was supplied in wire mesh containers. Neutrons appeared to be two to three times more effective than X rays in producing the lesions.

SUMMARY

The Problem:

A macroscopic lesion has been observed in the incisor teeth of rats several weeks after irradiation. Only one lesion per tooth is observed. This lesion is an area of structural weakness at which fracture may occur. A study was made to assess the incidence parameters for young adult male rats which develop the lesion after single whole body exposures to x-rays or neutrons in the high sublethal and lethal ranges.

The Findings:

At approximately 35 days following irradiation, the portions of the lower teeth containing the lesion began to emerge from the gums. Several weeks later, the lesions in the upper teeth emerged. The period of maximum incidence of animals with lesions was 50-75 days following either type of radiation. All lesions had disappeared through normal wearing of the continually growing incisor teeth at the biting edges by the end of the fourth month after irradiation. Almost all animals had a lesion in at least one tooth. At the higher radiation doses, the lesion was more pronounced, more teeth had a lesion and more fractures occurred. Supplying food in meal form resulted in a lower incidence of fractures compared with a previous study in which the same food was given in pellet form. Neutrons appeared to be two to three times more effective than x-rays in producing the dental lesions.

INTRODUCTION:

The literature on the radiobiology of the teeth of rats as well as other species has been reviewed recently (1). Radiation effects upon the continually growing incisor teeth of rats were first noted by Leist in 1925 (2). Leist's study, as well as most others in the interim, was concerned with the histologic evidence of radiation damage to ectodermal tissues. Inhibition of incisor growth (3) and the occurrence of multiple incisors (4) in head-exposed rats after large doses of x-rays have also been reported. More recently, a macroscopically visible lesion in intact incisors has been reported in a large number of rats after a sublethal dose of x-rays (5). The present report concerns the incidences of the lesion for several doses of two types of radiation and the time interval during which the lesion can be observed.

METHODS AND MATERIALS:

The animals were male Sprague-Dawley rats born in the USNRDC colony. They were caged individually and housed in air conditioned

quarters. Beginning within 35 days postirradiation, meal food (Purina Laboratory Chow) in open containers and water were supplied ad libitum.

The animals were part of a larger group destined to be studied throughout their life spans for late effects of irradiation. The study was composed of four experiments using animals from four birth-dates separated by two week intervals. Within each experiment, litter-mates were distributed as equally as practicable among a sham irradiated control group and two irradiated groups. The animals were exposed to a single dose of whole-body radiation at 101 days of age. Those in the first two experiments received 430 or 680 rads of x-rays; those in the third received 230 or 360 rads of neutrons and those in the fourth, 230 or 320 rads of neutrons. The radiation doses were selected to be high sublethal and midlethal doses. The 30 day survival rates for the x-ray groups were: 430 rads - 100%, 680 rads - 90% and for the neutron groups were: 230 rads - 100%, 320 rads - 90%, and 360 rads - 25%.

The radiation factors for the x-ray experiments were: 250 kVp, 15 ma, 3 filter, 0.5 mm Cu + 1.0 mm Al (WZ 2.5 mm Cu); T.S.D., 48 in. @ 27 r/min (air). The dose rate also was measured with a Victoreen chamber in a paraffin phantom and the total doses in rads were converted to rads by multiplying with a factor of 0.97. For exposure to the beam, the animals were placed in Lucite chambers arranged to approximate a lateral surface. The chambers were spaced radially on a motor-driven turntable which revolved slowly in the radiation field. The dorsal surfaces of the animals were nearest the x-ray tubes.

The 60 inch cyclotron of the University of California Crocker Laboratory was the source of fast neutrons. Neutrons were produced by 12 Mev proton bombardment of a beryllium target. Sulfur threshold detectors were used as dosimeters for the first collision dose. The neutron and gamma ray characteristics of this source (6) and the method of dosimetry (7) have been published. For exposure, each animal was confined to a cardboard tube placed with a lateral side toward the source. At the midpoint of the exposure, the tubes were turned 180° around the short axis to equalize the dose to each side of the animal.

After the first month postirradiation, the incisor teeth of each animal were inspected at approximately weekly intervals and diagrams were made of the observations to record the presence, position and approximate size of lesions and fractures. Prior to the appearance of the lesion, each tooth was probed gently to detect subgingival fracture. When an incisor was found to be fractured, the distal portion of the tooth was extracted. Rarely, a tooth was clipped to prevent soft tissue damage following fracture or extraction of its opposing member.

RESULTS:

Beginning approximately 35 days postirradiation, the radiation induced lesion became visible at the gingival crest in the continually growing mandibular incisors (Fig. 1). Similar lesions were borne to



Fig. 1 The incisor teeth of a rat that had been irradiated with 320 rads of neutrons 57 days previously. Note ~~that~~ white lesion in each of the mandibular incisors. The teeth are slightly constricted in the region of the lesion. The corresponding defects in the maxillary incisors are still subgingival.



Fig. 2 The incisor teeth of a rat that had been irradiated with 360 rads of neutrons 78 days previously. Note that each mandibular incisor is broken at the lesion, the remnant of which is at the occlusal surface. Each maxillary incisor is elongated as a result of fracture of its opposing incisor and is slightly constricted at the lesion.

view approximately two weeks later in the erupting maxillary incisors (Fig. 2). The lesion presented as a chalk-white zone in the maxillary and as a glassy to chalky zone in the mandibular incisors. The glassy appearance may have been due to the absence of pigmentation on the labial aspect of the tooth at that point. The size of the zone varied from a fine hair line to an area involving approximately 1/3 of the erupted tooth. The degree of visibility and the size of the zone varied with dose, being least after 430 rads of x-rays and greatest after 360 rads of neutrons. In some cases the shaft of the tooth was constricted at the lesion, the frequency being greater at the higher doses. In every instance the defective zone extended the full width of the tooth. The sizes of the lesions in adjacent teeth were not necessarily equal, differing, in some cases, by a factor of two.

The cumulative incidence of animals exhibiting one or more defective incisors was 97% in the 430-rad x-ray group and 100% in all other groups. There was a greater gradation of response with respect to number of incisors affected per animal among the sublethally x-irradiated animals than among those in the other groups. Defects were observed in all four incisors of 54% of those exposed to 430 rads of x-rays in contrast with 88% or more after all other x-ray and neutron doses. Although areas of discoloration are found occasionally on the incisor teeth of non-irradiated animals, in no instance has a lesion identical with that produced by irradiation been observed.

TABLE 1

PERCENT OF RATS WITH THE MACROSCOPIC RADIATION-
INDUCED LESION IN 0.4 INCISOR TEETH.

DOSE GROUP	N	NUMBER OF TEETH PER ANIMAL WITH LESIONS				
		0	1	2	3	4
X-Rays:		%	%	%	%	%
430 Rad	86	3	3	16	19	54
680 Rad	86	0	0	1	5	94
Neutrons:		%	%	%	%	%
230 Rad	58	0	2	3	3	33
320 Rad	53	0	0	0	2	98
360 Rad	16	0	0	0	7	93

The incidence of x-irradiated animals with one or more lesions as a function of time postirradiation is presented in Fig. 3. In both groups defective zones were detected initially between 35 - 45 days postirradiation. The maximum incidence was attained between days 50 - 65 in the 430 rad group and between days 50 - 75 in the 680 rad group. Lesions were no longer apparent by day 85 and day 105 in the 430 and 680 rad groups, respectively. The lesions were first observed in the mandibular incisors (Fig. 4) followed within two weeks by observation of lesions in the maxillary incisors of some animals. While the times of first appearance, maximum incidence and disappearance of mandibular lesions appeared to be about the same for both dose groups, a longer time was required for the incidence of animals with maxillary incisor lesions of the 680 rad group to reach a maximum and to return to zero.

The times of first appearance and of maximum incidence of neutron-exposed animals with lesions in the incisors (Fig. 5) corresponded to those observed for animals exposed to x-rays. For the earliest interval, the incidence in the 230 rad group was approximately four times that of either of the other two neutron-exposed groups and indicates a longer latency for comparable incidence with higher doses of neutrons. The maximum incidences observed were of the same order as that noted for the 680 rad x-ray group and occurred at approximately the same time. As in the case of the x-ray groups, the time required for disappearance of all lesions varied with dose. The dichotomy in

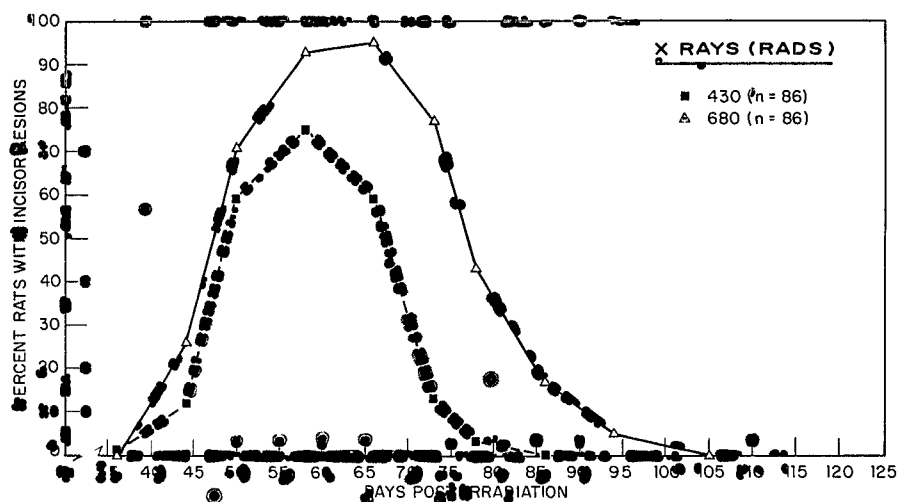


Fig. 3 Percent incidence of rats with incisor lesions, as a function of time, following whole-body x-irradiation.

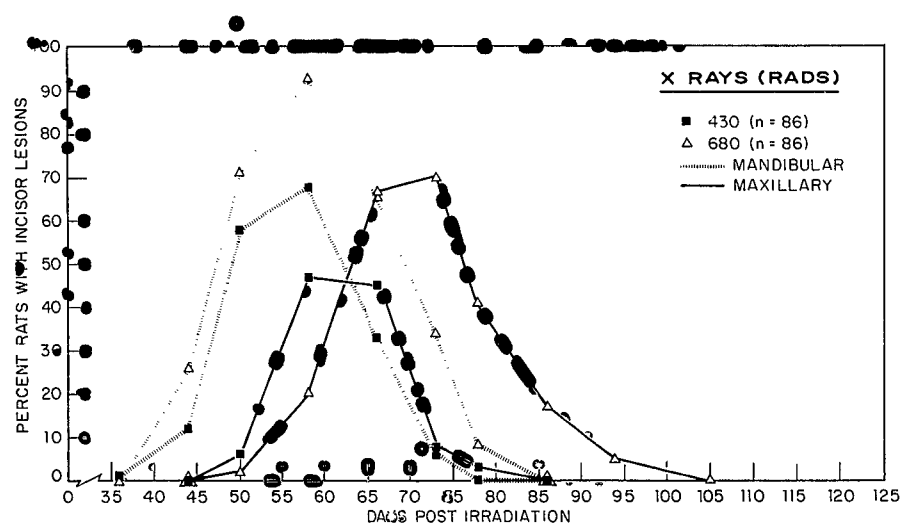


Fig. 4 Percent incidence of rats with lesions in mandibular and/or maxillary incisors, as a function of time, following whole-body x-irradiation.

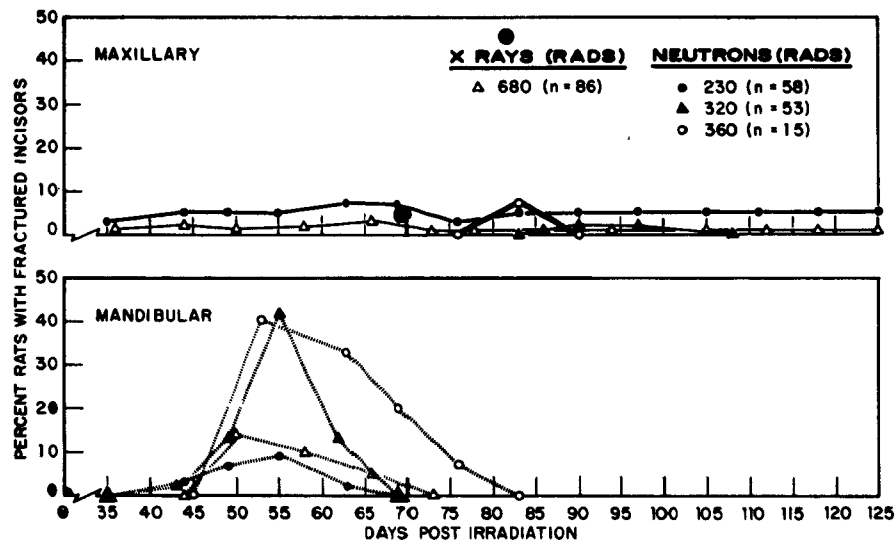


Fig. 3 Percent incidence of rats with broken mandibular and/or maxillary incisors, as a function of time, following whole-body neutron or x-irradiation.

For either mandibular or maxillary incisors, the initial appearance of a lesion occurred in the majority of the animals at the same time; however, there was an interval of three to five weeks before all animals in a group had presented a lesion. In those animals presenting a lesion of both mandibular or both maxillary incisors, the defective zone appeared in the second member of the pair within two weeks following appearance of a lesion in the first of the pair. For the individual animal, the time interval between the appearance of the defective zone in the first mandibular and the first maxillary incisor varied from less than a week to approximately seven weeks. The reason for the defect not appearing simultaneously in both of a pair of incisors is not known but may be due to differences in tooth bud-gingival crest distances, growth rates, and/or to cell state at irradiation. The same factors may also contribute to the variability in appearance times among animals. Unfortunately, there were insufficient numbers of littermates within each irradiation group to determine the portion of variability attributable to litter differences. An apparent genetic and/or neonatal effect upon mean day of first appearance of the lesion has been found (8).

In contrast with Leist's finding that maxillary incisors were damaged more often than mandibular incisors (2), it is of interest that the majority of our animals had lesions of all four incisors, and in those cases in which not all four incisors were affected, the

maxillary incisors were, in most instances, the ones without visible defects. Leist attributed his findings to the fact that his animals were irradiated from the dorsal side and assumed that the difference was due to a greater dose delivered to the maxillary incisors. In the present experiment the x-irradiated animals were also irradiated from the dorsal side. The inconsistency in the observations may lie in differences in the energy spectra of the radiation beams and the resultant differential in depth dose.

In a previous experiment (5) in which food pellets were presented in containers of wire mesh through which the animals had to gnaw, the incidence of animals with fractures was 26% after 430 rads and 91% after 680 rads of x-rays. In that study, the animals were given meal food as well as pellets in open containers only after detection of a broken tooth. In the present study, in which the animals were placed on meal food within 35 days following irradiation, the fracture incidences were 1% after 430 rads and 31% after 680 rads. The considerable differences in incidences are, no doubt, due to the manner of feeding. These observations suggest the value of preventive measures in studies of irradiated rats during the critical dental period. It would be advantageous to preclude partial or total starvation during the critical dental period by feeding the animals meal food in open containers and inspecting the teeth at least once a week. Contrary to opinions held by some, the

rat does not appear to require pellet food upon which to gnaw in order to prevent overgrowth of incisor teeth. Our present practice is to maintain animals on meal food from the time of receipt from the breeding colony (25 days of age) until death. Animals have been maintained on this regimen for more than 1000 days without dental problems arising as a result of the physical state of the food.

The critical dental period may not coincide in all cases with that presented here. The time of appearance of defective tooth substance in the exposed portion of the incisor may be delayed at higher doses. For example, Medak et al (9) have published photomicrographs of maxillary incisors in which the defective portion of the tooth had not erupted at 27 and 30 weeks following local exposure to 3000r of 100 kv x-rays. It is possible that some of the broken teeth observed in the present study were the result of a transient complete cessation of tooth formation with a resultant minute gap in the tooth structure similar to the more pronounced gaps observed following exposure of the head only to single (4,9) or multiple (10) doses of kiloroentgen magnitude.

The fractures in the present experiment were confined largely to the mandibular incisors. Although this may be due to a greater degree of radiation damage to the lower incisors, it may also be a resultant of the differences in physical characteristics between the two pairs of teeth. The smaller cross section, the greater length and the

apparent lesser support by its pair member as evidenced by lateral mobility, are factors which would favor fracture of the mandibular incisor.

SUMMARY:

Adult male rats were exposed to single whole-body doses of x-rays or neutrons in the high sublethal and 30 day lethal ranges. A chalky zone was detected in the tooth shaft at the gingival crest of mandibular incisors approximately 35 days postirradiation and in maxillary incisors several weeks later. The intensity of the lesion and the number of incisors affected per animal varied with dose being least after sublethal x-irradiation and greatest after exposure to neutron doses in the lethal range. The lesions were no longer apparent after the fourth postirradiation month. Fractured incisors were observed during the same period, the number of animals with fractures being greater after higher doses. Fractures were predominantly in mandibular teeth. The use of meal food in open containers markedly reduced the incidence of fractures. Neutron irradiation appears to be two to three times more effective than x-rays in producing the defects described.

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